

FIG. 2F

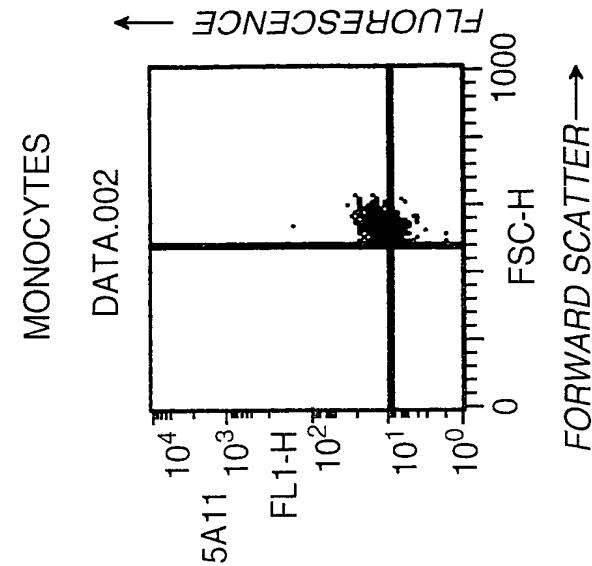


FIG. 2E

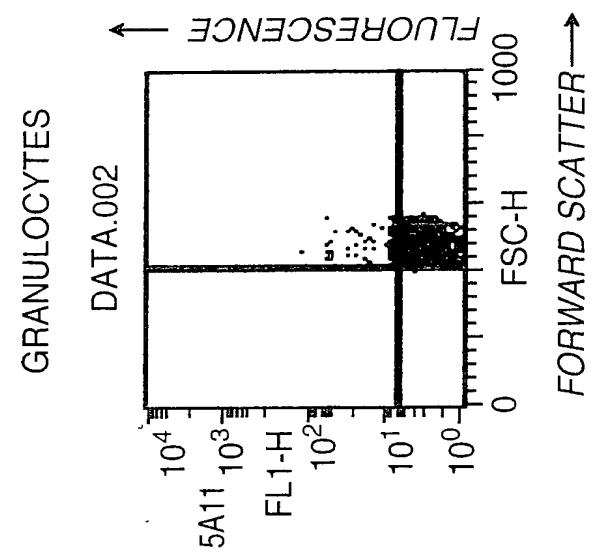


FIG. 2D

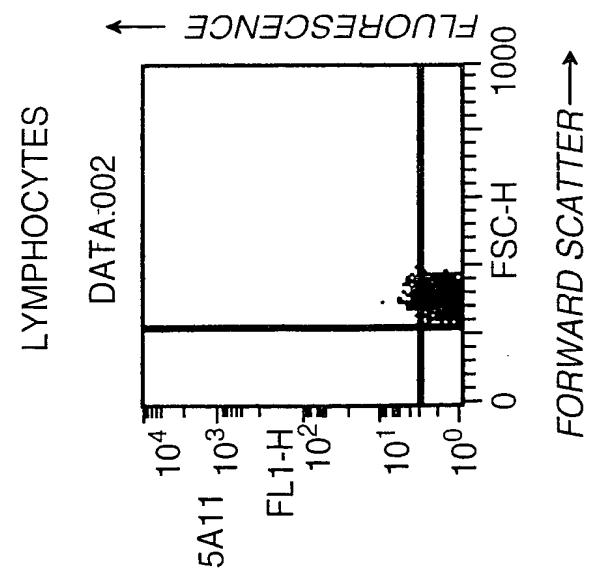


FIG. 2G

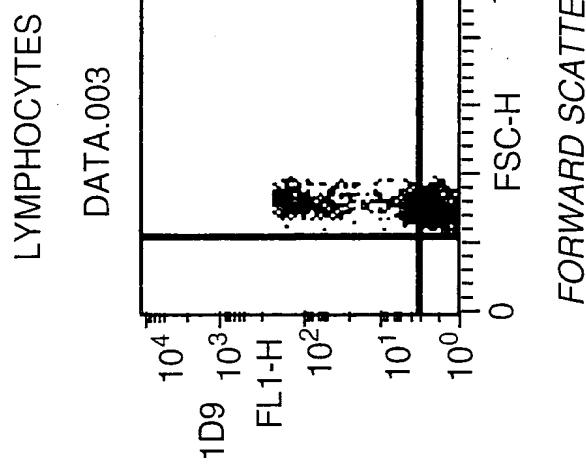


FIG. 2H

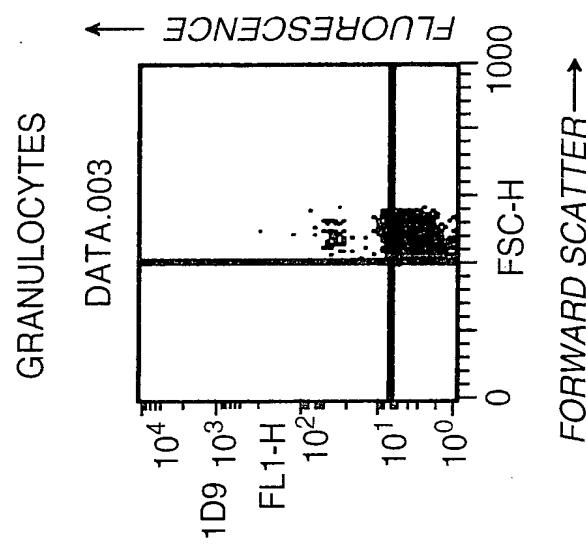


FIG. 2I

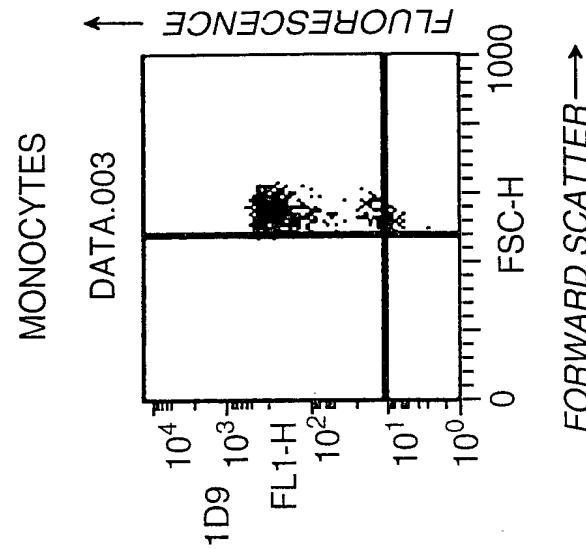


FIG. 2L

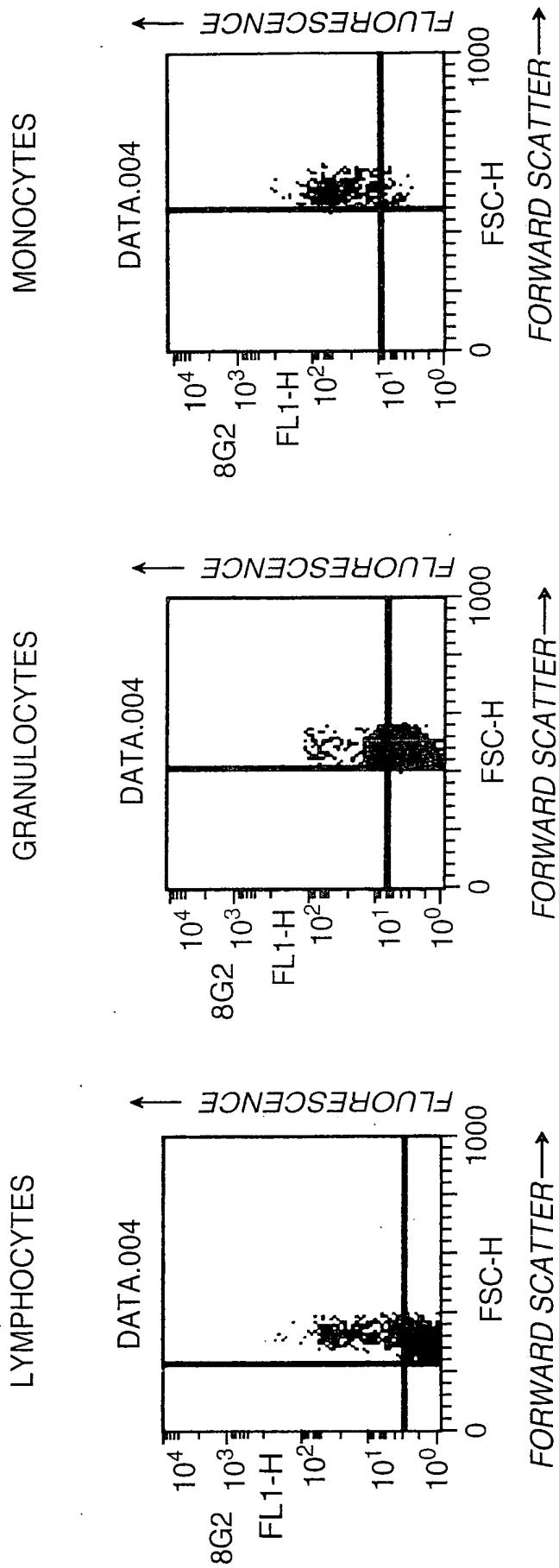


FIG. 3A

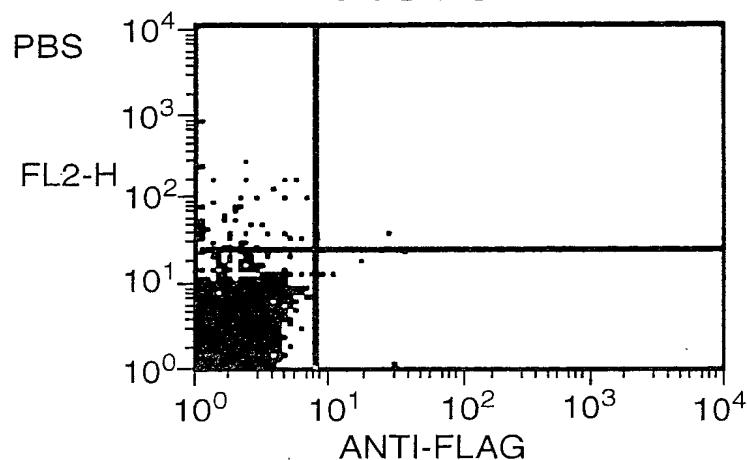


FIG. 3B

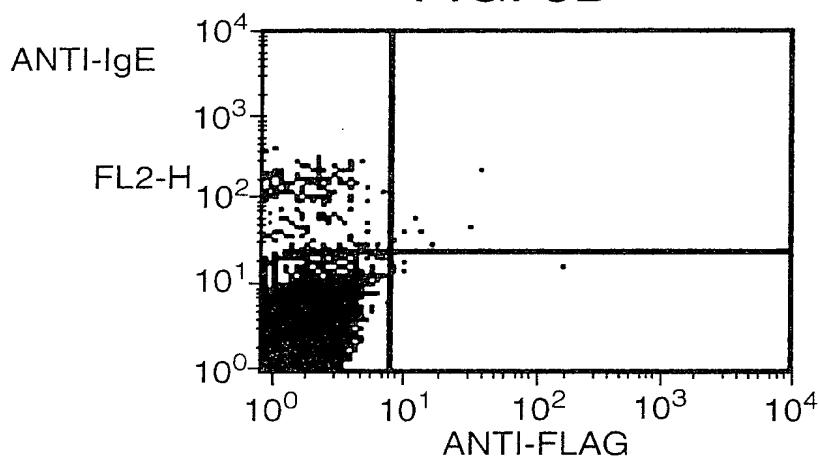


FIG. 3C

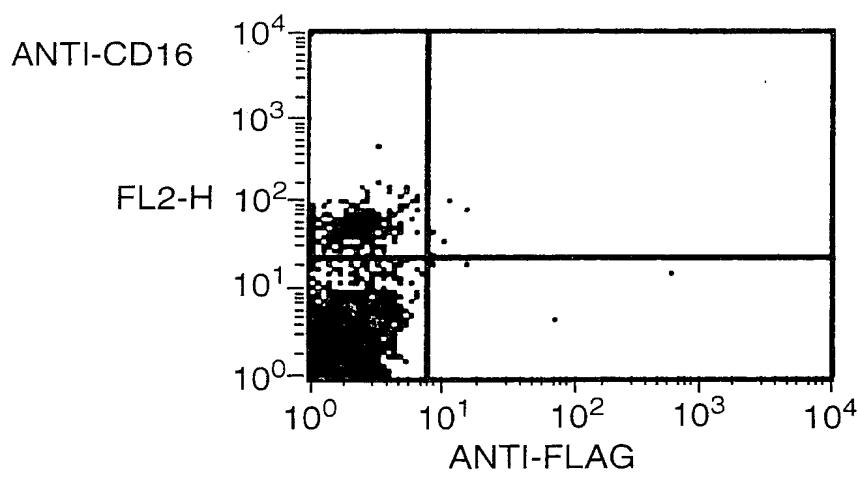


FIG. 3D

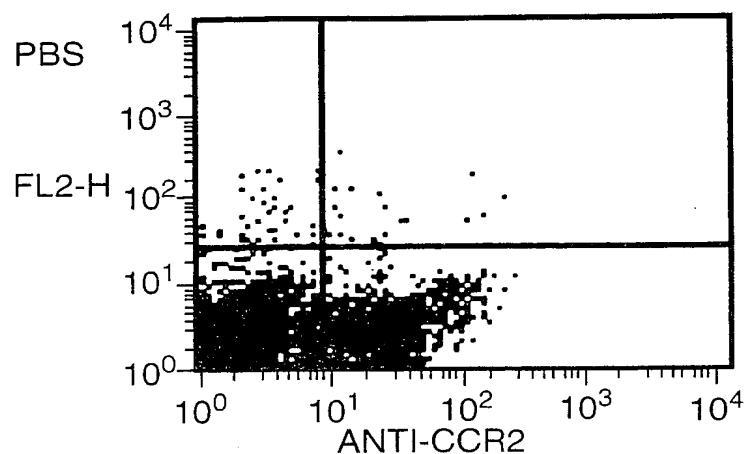


FIG. 3E

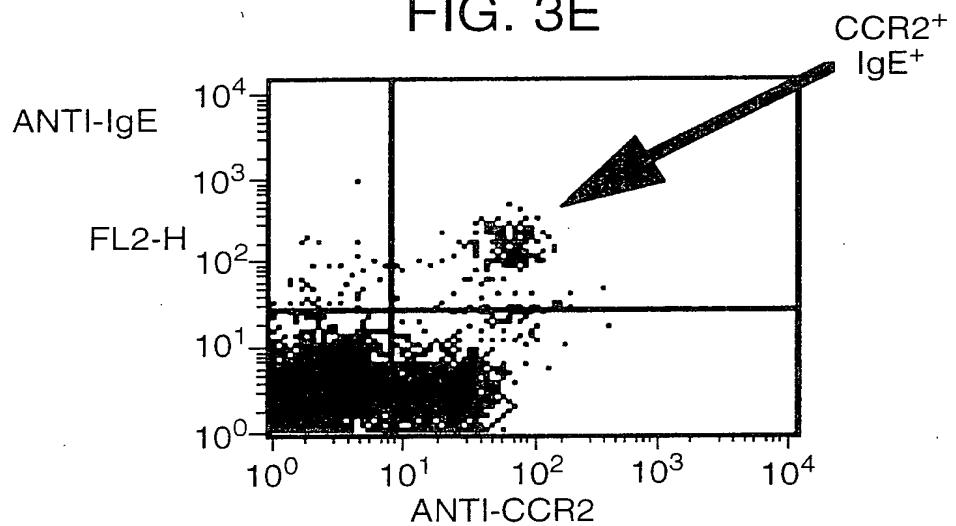


FIG. 3F

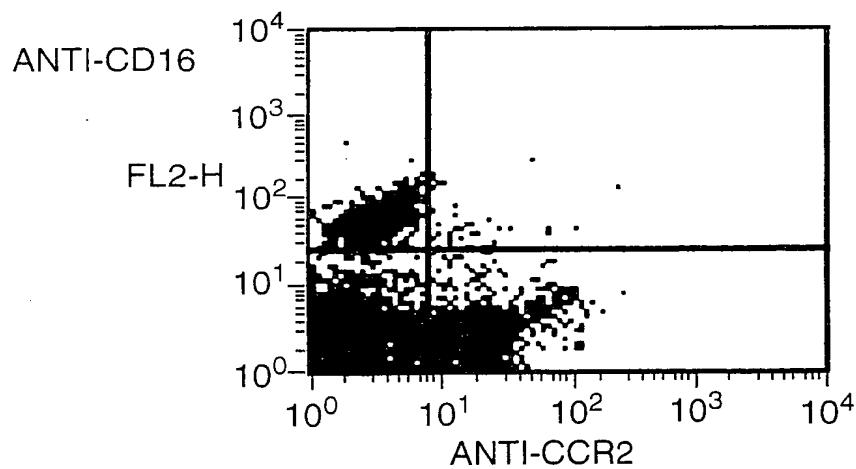


FIG. 3G

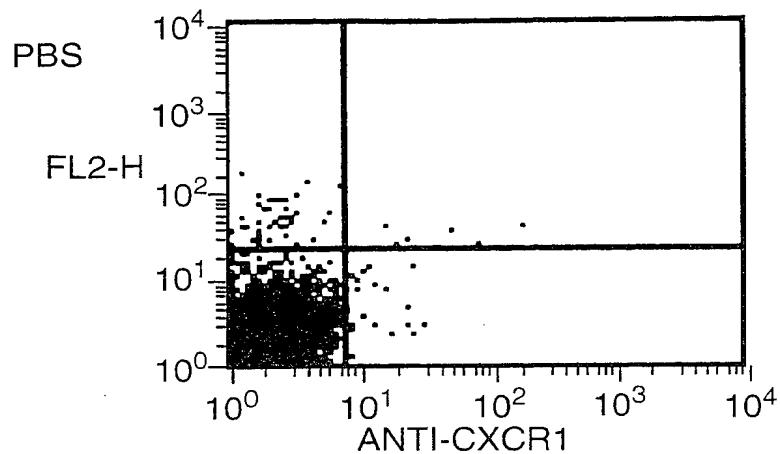


FIG. 3H

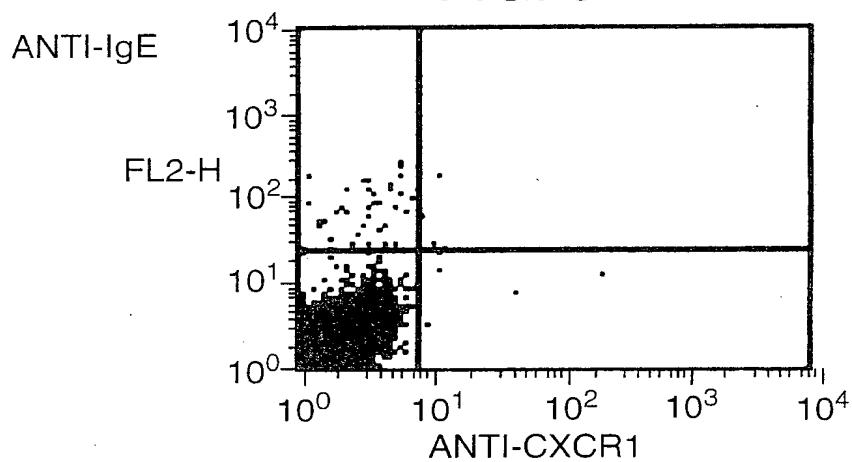
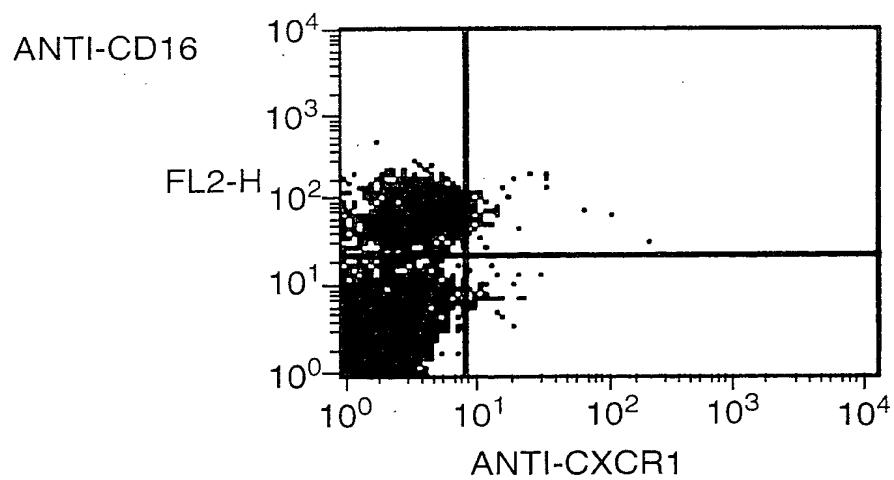
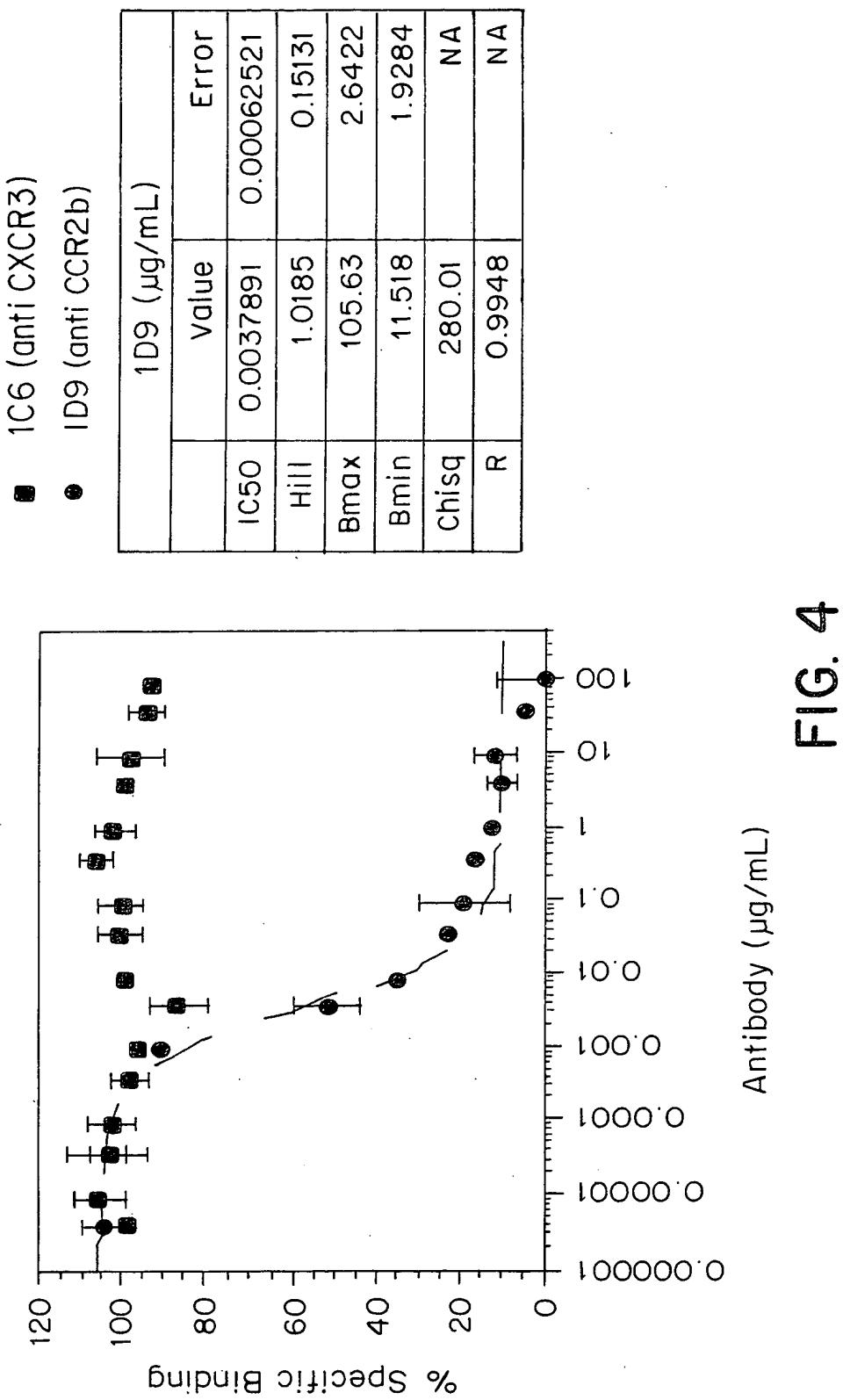


FIG. 3I





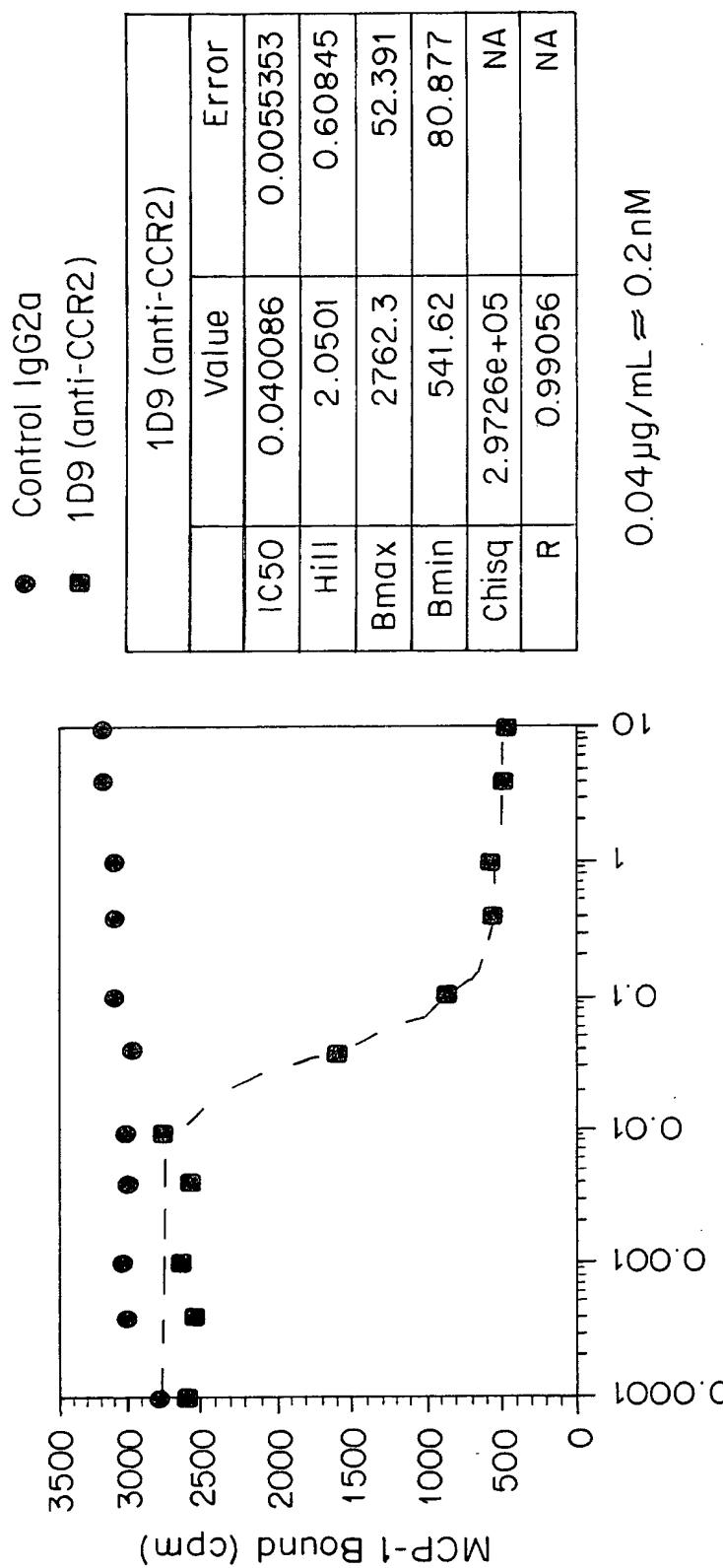


FIG. 5

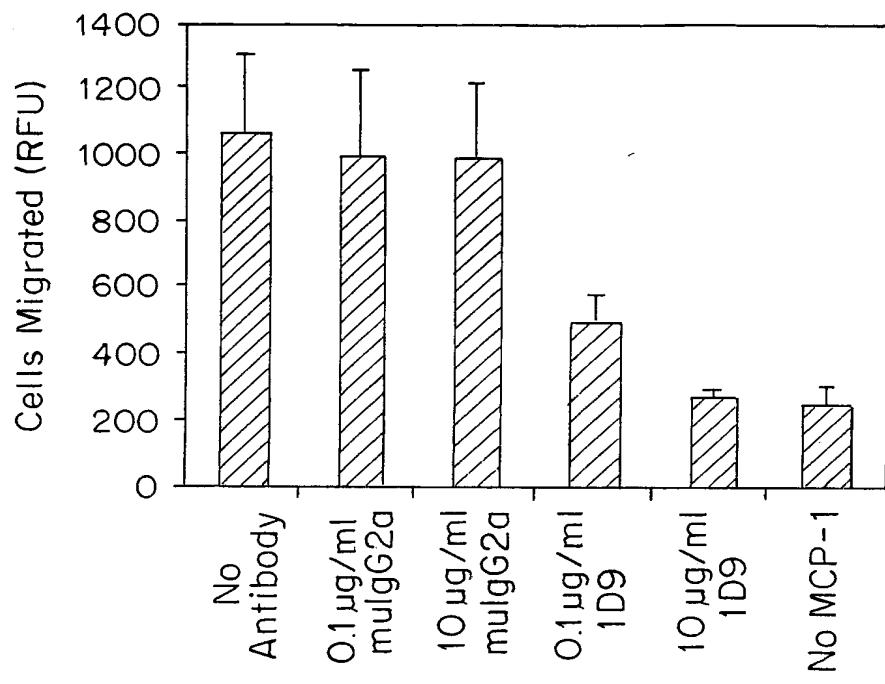


FIG. 6A

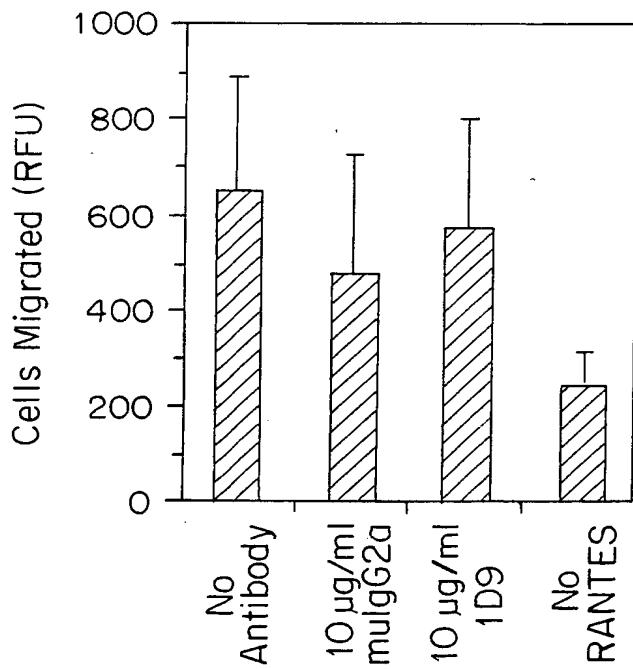


FIG. 6B

Docket No.: 1855.1052-028
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, *et al.*

1 DVVMTQTPLT LSVTVGHPAS ISC**KSSQSLL** DSDGKTFLNW LLQRPGQSPK

51 RLIY**LVS**KLD SGVPDRFTGS GSGTDFTLKI SRVEAEDLGV YYC**WQGTHFP**

101 **YT**FGGGTKLE IK

Figure 7

Docket No.: 1855.1052-028
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, et al.

1 EVQLVESGGG LVQPKGSLKL SCAASGFSFN **AYAMN**WVRQA PGKGLEWVAR

51 IRTKNNNYAT YYADSVKDRY TISRDDSESM LFLQMNNLKT EDTAMYVCVT

101 **FYGN**GVWGTG TT VTVSS

Figure 8

Docket No.: 1855.1052-028
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, et al.

Chothia Canonical Classes

- | | |
|---------------------|--|
| L1 (16 amino acids) | = Class 4 Key residues: 2(V), 25(SA), 29(L), 33(L), 71(F) |
| L2 (7 amino acids) | = Class 1 Key residues: 48(IV), 51(AT), 52(ST), 64(G) |
| L3 (9 amino acids) | = Class 1 Key residues: 90(QNH), 95(P) |

Martin Canonical Classes

- L1 (16 amino acids) = Class 4/16A
 Key residues: **2(V), 4(ML), 23(C), 25(SSP), 26(SN),**
 27(Q), 29(LI), 30A(HL), 30B(S),
 30C(NDS), 30D(G), 32(YS), 33(LF),
 34(HEN), 35(W), 51(V), 71(F), 88(C),
 90(Q), 92(TS), 93(H)

L2 (7 amino acids) = Class 1/7A
 Key residues: **23(C)**

L3 (9 amino acids) = Class 1/9A
 Key residues: **2(ILV), 3(VQLE), 4(ML),**
 28(SNDTE), 30(DYLVISNFGHT),
 31(SNTKG), 32(FYNAHSR),
 33(MLVIF), 88(C), 89(QSGFL),
 90(QNH), 91(NFGSRDHTYV),
 92(NYWTSRQHAD),
 93(ENGHTSRAQHAD),
 94(DYTQLHNNIWPS), 95(P),
 96(PLYRIWF), 97(T), 98(F)

Figure 9

Chothia Canonical Classes

H1 (5 amino acids) = Class 1
Key residues: 24(AVG), 26(G), 27(FY)

H2 (19 amino acids) = Class 4
 Key residues: 54(S), 55(Y), 71(R)

Martin Canonical Classes

H1 (5 amino acids) = Class 1/10A
 Key residues: 2(VIG), 4(LG), 20(LIMV), 22(C),
 24(TAGVS), 26(G), 29(IFLS),
 32(IHYFTNCED), 33(AWGTLV),
 34(IVMW), 35(HENQSYT), 36(W),
 48(IMLV), 51(LIVTSN),
 69(ILFMV), 78(ALVYF), 80(LM),
 90(YF), 92(C), 94(RKGSNH),
 102(YHVISDG).

H2 (19 amino acids) = Class ?/12B
Key residues: 47(W), 50(RQ), 51(I), 59(Y), 69(I),
71(R), 78(LV)

Figure 10

Docket No.: 1855.1052-028
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, et al.

Key

- | | |
|-----------------------------------|--|
| 1D9 V _H | Mouse 1D9 V _H region. |
| 4B4'CL V _H | Chosen human framework acceptor V _H region sequence with mismatches to the 1D9 V _H |
| 1D9RH _A V _H | CDR grafted 1D9 V _H region, with no back mutations. |
| 1D9RH _B V _H | CDR grafted 1D9 V _H region, with back mutations at T28S and S30N. |
| 1D9RH _C V _H | CDR grafted 1D9 V _H region, with back mutations at T28S, S30N, G49A and F67Y. |
| 1D9RH _D V _H | CDR grafted 1D9 V _H region, with back mutations at T28S, S30N, G49A, F67Y and T93V. |

Figure 12

Sequence Name Identical Residues Amino Acid Sequence

| 1D9 V _κ | 114 | DVVMQTPLTISVTIVGHDPASISCKSSQSLIDS-DGKTEFLINWLLQRPGQSPKRLIYLVSKLDSGVPDFGSGGTDFTLKISRVEAEDLGVYYCWQGTHFP |
|--------------------|-----|--|
| 70/3 | 97 |I.Q.....Y.....Y.....Y.....N.....Y.....Y.....V.P.....Y.....S.....Y.....S.....V..... |
| 70/1 | 94 |I.Q.....Y.....Y.....N.....Y.....Y.....V.P.....Y.....S.....Y.....S.....X.P.....X.M.D..... |
| 70/2 | 82 |XLHS.....I.Q.....Y.....VH.....N.N.Y.Y.Y.....K.....L.....R.....NRF.....S.....F.F.....V. |
| V-IB | 76 |S.P.SL.DQ.....R.....VH.....N.N.Y.Y.Y.....K.....L.....R.....NRF.....S.....F.F.....S.V. |
| V-1C | 75 |S.P.SL.DQ.....R.....IVH.....N.N.Y.E.Y.....K.....L.....K.....NRFL.....S.....F.S.S..V. |
| V-1A/K5.1/K5.1 | 75 |S.P.SL.DQ.....R.....VH.....N.N.Y.H.Y.....K.....L.....K.....NRFL.....S.....F.S.S..V. |
| V-1C/V1A5/K1A5 | 74 | ..L.....S.P.SL.DQ.....R.....IVH.....N.N.Y.E.Y.....K.....L.....K.....NRF.....S.....F..S.V. |
| K18.1 | 73 | ..A.....S.P.SL.DQ.....R.....EN.....N.N.Y.Y.....K.....QL.....R.....NRF.....L.....S.....F.L.V..V. |
| 1F | 71 | ..LL.....F.P.SL.DQ.....S.....VH.....N.NYY.E.H.....KS.....LQL.....E.....RH.....S.....P.....F....L. |
| 24A | 68 | .I.....AAFSNP..L.TS.....R.....K.....H.....S.N.Y.Y.F.....K.....QL.....YI.N.A.....S.....R.....V.....M..LEY. |
| 167/24 | 67 | .I.I.....DE.SNP..S.ESV.....R.....K.....YK.....Y.....F.....QL.....M.TRA.....S.....S.....E.....K.....V.....Q.LVEY. |
| 24B | 66 | .I.....AAFSNP..L.TS.....R.....K.....H.....N.I.Y.Y.Y.....K.....QL.....QM.N.A.....S.....R.....V.....A.NLEL. |

Figure 13

Sequence Name Identical Residues Amino Acid Sequence

| | | |
|--------------------|-----|--|
| 1D9 V _H | 117 | EVQLINEGGGLVQPKGSILKLSCCAASGFSPNAYAMN--WVRQAPGKGLEWVARITKNNNYATYADSVVKDRYTISRDDSESMFLQMNNLKTEDTAMYYCVTF |
| MRL-REF24BG | 86 |VWWRM.....T.....T.....F.....Q.....Y.....I- |
| V(H)22.1 | 70 | ..K.E.....G.M.....V....T.SN.W.S.....S.E.....Q.....L.SD.....H.E.....G.F.....K.SVY.....RA.....GI.....TG- |
| V11/pBV19B4 | 66 | ..K.....G...R.....T.....T.TD.Y.S.....P...A...LGF.N.A.G.T.E.SA.....G.F.....N.Q.I.Y.....T.RA.....S.T...AR- |
| Vh7183 (Vh69.1) | 66 | ..K.....K.G.....T.SS.T.S.....S.E.R.....T.SS--GGSY...P.....G.F.....NAKNT.Y.....SS.....S.....TR- |
| VH10-19 | 65 | D.K.....K.G.....T.SS.T.S.....T.E.R.....T.SS--GGSY...P.....G.F.....NAKNT.Y.....SS.....S.....TR- |
| VHE4-psi | 65 | L.....G...R.....T.SS...S.....T.E.R.....A.S--DGSEFI.XP.T.....G.F.....NAKNT.Y.....SS.RY.....LR- |
| V(H)50.1 | 65 | ..K.....G.....T.....T.SD.Y.Y.....T.E.R.....Y.SN--GGGS...P.T.....G.F.....NAKNT.Y.....SR.....S.....AR- |
| V3 | 65 | ..K.....GA...R.....S.....T.TD.Y.....HRP...P.....L.L.N.A.G.I.E.SA.M.G.F.....N.Q.I.Y.....T.S.....S.T...ARD |
| V1/pBV132 | 64 | ..K.....G...R.....T.....T.SDFY.E.....P...R.....I.AS.N.A.D.T.E.SA.....G.FIV...T.Q.I.Y.....A.RA.....I...AR- |
| VH283 | 64 | .M.....K.G.....T.SS.T.S.....T.E.R.....T.SS--GGGN...P.....G.F.....NAKNN.Y.....SS.RS.....L...AR- |
| V(H)37.1 | 63 | ..K.....K.G.....T.....T.SS.G.S.....T.E.R.....T.SG--GGSY...P.....G.F.....NAKNN.Y.....SS.RS.....L...AR- |
| V13 | 61 | ..K.M.....GA...R.....E.....T.TD.Y.S.....L.R.SP.....L.L.N.A.G.T.E.SA.....G.F.....N.QN.I.Y.....T.RA...AS.T...AKD |
| V-H_441/V441 | 59 | ..K.L.....G.....D.SR.W.S.....IGE.NP--DSSTIN.TP.L..KFI.....NAKNT.Y.....SKVRS.....L...AR- |
| 68-5N | 59 |G.....T.SS.G.S.....T.D.R.....L.T.NS--GGS...P.....G.F.....NAKNT.Y.....SS.....S.....AR- |
| 76-1BG/VH7183.9 | 58 |K.G.....T.SS...S.....T.E.R.....T.SS--GGSY...P.....G.F.....NAKNT.Y.....SS.RS.....AR- |
| 61-1P | 58 |G...R.....T.SSTG.H.....E.....Y.SS--GSSTI.....T.....G.F.....NPKN....TS.RS.....AR- |
| 57-1M/VH7183.12 | 58 |K.G.....T.SS...S.....T.E.R.....S.S--SGGS...P.....G.F.....NARNI.Y.....SS.RS.....AR- |
| V(H)55 | 56 | ..K.L.....G...N.....D.SR.W.S.....A.....Q.....IGE.NP--GSSTIN.TP.L..KFI.....NAKNT.Y.....SKVRS.....L...AR- |
| VH7183.13 | 55 |K.G.....T.SS.T.S.....T.E.R.....Y.SN--GGGS...P.T.....G.F.....NAKNT.Y.....SS.....S.....AR- |

Figure 14

Figure 15

| Name | ID | Surface | Core | Kabat | FR | FR | Core | Vernier | V _k | J | Closest Human | L1 | L2 | L3 |
|--------------------|-------|---------|------|-------|---------|----|------|---------|----------------|-------|---------------|---------------|-------|-------|
| | | | | CDR | Surface | FR | Near | Chain | Germline Gene | Class | Class | Class | Class | Class |
| | | | | CDR | | | | | | | | | | |
| 1D9 V _k | 100.0 | 30 | 82 | 32 | 82 | 22 | 60 | 33 | 14 | 100 | 14 | 16 | 7 | 9 |
| 036521 | 90.4 | 27 | 76 | 28 | 75 | 19 | 56 | 31 | 13 | 90 | 13 | DPK19-A1+ | Same | Same |
| II.66 | 78.8 | 25 | 67 | 22 | 69 | 18 | 52 | 30 | 13 | 80 | 12 | DPK18-A17+ | Same | Same |
| RPMI6410 | 78.8 | 25 | 67 | 22 | 69 | 18 | 52 | 30 | 13 | 79 | 12 | DPK18-A17+ | Same | Same |
| ZM1-1 | 78.8 | 25 | 66 | 21 | 68 | 18 | 52 | 30 | 13 | 79 | 12 | DPK18-A17+ | Same | Same |
| VL clone | 78.1 | 25 | 66 | 21 | 68 | 18 | 52 | 30 | 13 | 79 | 12 | DPK18-A17+ | Same | Same |
| 54 | | | | | | | | | | | | | ? | Same |
| HF-21/28 | 79.3 | 24 | 66 | 21 | 68 | 18 | 52 | 30 | 13 | 78 | 12 | DPK18-A17+ | Same | Same |
| SpA2-08 | 77.9 | 24 | 65 | 21 | 68 | 18 | 51 | 30 | 13 | 77 | 12 | DPK18-A17+ | Same | Same |
| II.30 | 77.9 | 24 | 65 | 21 | 68 | 18 | 51 | 30 | 12 | 77 | 12 | DPK18-A17+ | Same | Same |
| HUNVK | 77.9 | 24 | 65 | 21 | 68 | 18 | 51 | 30 | 12 | 77 | 12 | DPK18-A17+ | Same | Same |
| O-81 | 75.7 | 24 | 65 | 21 | 68 | 18 | 51 | 30 | 12 | 77 | 12 | DPK18-A17+ | Same | Same |
| ToP309 | 74.8 | 24 | 64 | 20 | 68 | 18 | 51 | 29 | 12 | 76 | 12 | DPK12-A2+ | Same | Same |
| ToP218 | 74.8 | 24 | 64 | 20 | 68 | 18 | 51 | 29 | 12 | 76 | 12 | DPK12-A2+ | Same | Same |
| SpA3-02 | 76.1 | 24 | 63 | 20 | 68 | 18 | 51 | 29 | 12 | 76 | 12 | DPK18-A17+ | Same | Same |
| II.37 | 75.2 | 24 | 63 | 20 | 68 | 18 | 51 | 29 | 12 | 76 | 12 | DPK18-A17+ | Same | Same |
| CUM | 73.9 | 24 | 63 | 20 | 68 | 18 | 50 | 29 | 12 | 75 | 12 | DPK36-Chr22 4 | 17 | Same |
| VL clone | 74.6 | 24 | 62 | 20 | 67 | 18 | 50 | 29 | 12 | 75 | 12 | DPK18-A17+ | Same | Same |
| 51 | | | | | | | | | | | | | ? | Same |
| II.20 | 75.2 | 23 | 62 | 20 | 67 | 18 | 50 | 29 | 12 | 75 | 12 | DPK18-A17+ | Same | Same |
| | | | | | | | | | | | | | ? | Same |

Figure 16

Figure 17A

Amino Acid Sequence

Figure 17B

| Name | ID | All | Surface | Core | Kabat | FR | FR | Core | FR | Vernier | V _H | J Chain | Closest Human Germline Gene | H1 Size | H2 Size | H3 Size | Class | Class |
|--------------------|-------|-----|---------|------|-------|----|----|------|----|---------|----------------|---------|-----------------------------|---------|---------|---------|-------|-------|
| 1D9 V _H | 100.0 | 117 | 29 | 84 | 30 | 87 | 21 | 65 | 30 | 16 | 100 | 17 | | 5 | 19 | 6 | 1 | 4 |
| 030094 | 67.7 | 86 | 19 | 67 | 15 | 72 | 17 | 57 | 26 | 12 | 75 | 13 | DP-29-122+ | Same | Same | 16 | Same | Same |
| N51P8 | 68.3 | 86 | 18 | 66 | 15 | 72 | 16 | 57 | 25 | 12 | 75 | 13 | DP-29-122+ | Same | Same | 15 | ? | Same |
| IW2-91 | 67.5 | 85 | 18 | 65 | 15 | 72 | 16 | 56 | 25 | 12 | 75 | 12 | DP-29-122+ | Same | Same | 15 | Same | Same |
| H2-46 | 66.7 | 84 | 18 | 65 | 15 | 72 | 16 | 56 | 25 | 12 | 75 | 12 | DP-29-122+ | Same | Same | 15 | Same | Same |
| 039158 | 72.2 | 83 | 17 | 64 | 15 | 71 | 15 | 56 | 25 | 12 | 74 | 12 | DP-29-122+ | Same | Same | 15 | Same | Same |
| 038064 | 65.6 | 82 | 17 | 64 | 14 | 71 | 15 | 56 | 25 | 11 | 74 | 12 | VH26Rabbits+ | | | | | |
| 038062 | 64.6 | 82 | 17 | 63 | 14 | 71 | 15 | 56 | 25 | 11 | 73 | 12 | VH26Rabbits+ | | | | | |
| 32.B9 | 64.6 | 82 | 17 | 63 | 14 | 71 | 15 | 56 | 25 | 11 | 72 | 12 | VH26Rabbits+ | | | | | |
| 038062 | 64.6 | 82 | 17 | 63 | 14 | 71 | 15 | 56 | 25 | 11 | 72 | 12 | VH26Rabbits+ | | | | | |
| 034514 | 69.8 | 81 | 17 | 63 | 14 | 70 | 15 | 56 | 25 | 11 | 72 | 12 | VH26Rabbits+ | | | | | |
| 038066 | 65.3 | 81 | 16 | 63 | 14 | 70 | 15 | 55 | 25 | 11 | 71 | 12 | VH26Rabbits+ | | | | | |
| 035365 | 65.9 | 81 | 16 | 63 | 14 | 70 | 15 | 55 | 25 | 11 | 71 | 12 | VH26Rabbits+ | | | | | |

Figure 18A

| Name | ID | All | Surface | Core | Kabat | FR | FR | Core | FR | Vernier | V_H | J Chain | Closest Human | H1 | H2 | H3 | H1 | H2 | |
|----------|--------|------|---------|------|-------|---------|----|------|-----|---------|-------|---------|---------------|-------------|------|------|-------|-------|---|
| | | | | | CDR | Surface | FR | Near | CDR | | | | Germline Gene | Size | Size | Size | Class | Class | |
| Hb-5 | 69.2 | 81 | 16 | 63 | 14 | 69 | 15 | 55 | 25 | 11 | 71 | 12 | VH26Rabbits+ | Same | 17 | 16 | Same | 3 | |
| 4G12 | 64.8 | 81 | 16 | 63 | 14 | 69 | 15 | 55 | 25 | 11 | 71 | 12 | VH26Rabbits+ | Same | 17 | 11 | Same | 3 | |
| VH clone | 66.7 | 80 | 16 | 63 | 14 | 69 | 14 | 55 | 25 | 11 | 71 | 12 | VH26Rabbits+ | Same | 17 | 11 | Same | 3 | |
| 39 | 040094 | 62.5 | 80 | 16 | 63 | 14 | 69 | 14 | 55 | 25 | 11 | 71 | 12 | LSG3.1 | Same | 17 | 18 | Same | 3 |
| VH clone | 63.0 | 80 | 16 | 63 | 13 | 69 | 14 | 55 | 25 | 11 | 71 | 12 | VH26Rabbits+ | Same | 17 | 18 | Same | 3 | |
| 18 | UB1-24 | 67.2 | 80 | 16 | 63 | 13 | 69 | 14 | 55 | 25 | 11 | 71 | 12 | DP-31-V39P+ | Same | 17 | 10 | Same | 3 |
| 029764 | 64.5 | 80 | 16 | 63 | 13 | 69 | 14 | 55 | 25 | 11 | 71 | 12 | VH26Rabbits+ | Same | 17 | 15 | Same | 3 | |
| IW2-105 | 64.5 | 80 | 16 | 63 | 13 | 69 | 14 | 55 | 25 | 11 | 71 | 12 | LSG3.1 | Same | Same | 13 | Same | ? | |
| UB1-17 | 65.0 | 80 | 16 | 63 | 13 | 69 | 14 | 55 | 25 | 11 | 71 | 11 | LSG3.1 | Same | Same | 12 | Same | ? | |
| VH clone | 66.1 | 80 | 16 | 62 | 13 | 69 | 14 | 55 | 25 | 11 | 71 | 11 | VH26Rabbits+ | Same | 17 | 12 | Same | 3 | |
| 41 | 4B4'CL | 67.2 | 80 | 16 | 62 | 13 | 68 | 14 | 55 | 25 | 11 | 71 | 11 | LSG3.1 | Same | Same | 8 | Same | ? |
| M26 | 65.0 | 80 | 16 | 62 | 13 | 68 | 14 | 55 | 25 | 11 | 71 | 11 | LSG3.1 | Same | Same | 12 | Same | ? | |

Figure 18B

| Kabat | # | FR or CDR | Mouse 1D9 V _K | Mouse κ-II | Human κ-II | Human Acceptor HF-21/28 (005056) | Surface or Core | | 1D9 RK _A | 1D9 RK _B | Comment |
|-------|----|-----------|--------------------------|------------|------------|----------------------------------|-----------------|--|---------------------|---------------------|---------|
| 1 | 1 | FR1 | D | D* | D | | S | | D | D | |
| 2 | 2 | | V | V | I* | | C | | V | V | |
| 3 | 3 | | V | V | V* | | S | | V | V | |
| 4 | 4 | | M | M | M | | C | | M | M | |
| 5 | 5 | | T | T* | T | | C | | T | T | |
| 6 | 6 | | Q | Q* | Q | | C | | Q | Q | |
| 7 | 7 | | T | T | S | S | S | | S | S | |
| 8 | 8 | | P | P | P | | c | | P | P | |
| 9 | 9 | | L | L | L | | s | | L | L | |
| 10 | 10 | | T | S | S | S | C | | S | S | |
| 11 | 11 | | L | L | L* | | c | | L | L | |
| 12 | 12 | | S | P | P | P | c | | P | P | |
| 13 | 13 | | V | V* | V* | V* | c | | V | V | |
| 14 | 14 | | T | S | T | | c | | T | T | |
| 15 | 15 | | V | L | P | L | s | | L | L | |
| 16 | 16 | | G | G | G | | c | | G | G | |
| 17 | 17 | | H | D | E | Q | c | | Q | Q | |
| 18 | 18 | | P | Q | P | | s | | P | P | |
| 19 | 19 | | A | A | A | | c | | A | A | |
| 20 | 20 | | S | S* | S | | c | | S | S | |
| 21 | 21 | | I | I* | I | | c | | I | I | |
| 22 | 22 | | S | S* | S* | | C | | S | S | |
| 23 | 23 | FR1 | C | C | C | | C | | C | C | |
| 24 | 24 | CDR1 | K | R | R | R | s | | K | K | |
| 25 | 25 | | S | S* | S* | | c | | S | S | |
| 26 | 26 | | S | S* | S | | s | | S | S | |
| 27 | 27 | | Q | Q | Q | | s | | Q | Q | |
| 27A | 28 | | S | S | S | | s | | S | S | |
| 27B | 29 | | L | L | L | | c | | L | L | |
| 27C | 30 | | L | V | L | V | s | | L | L | |
| 27D | 31 | | D | H | H | H | c | | D | D | |
| 27E | 32 | | S | S | S | | s | | S | S | |
| 27F | | | - | | x | | | | - | - | |
| 28 | 33 | | D | N | D | | s | | D | D | |
| 29 | 34 | | G | G* | G | | c | | G | G | |
| 30 | 35 | | K | N | N | N | c | | K | K | |
| 31 | 36 | | T | T | N | | c | | T | T | |
| 32 | 37 | | F | Y* | Y | Y | c | | F | F | |
| 33 | 38 | | L | L* | L | | c | | L | L | |
| 34 | 39 | CDR1 | N | E | N | | c | | N | N | |
| 35 | 40 | FR2 | W | W | W | | C | | W | W | |
| 36 | 41 | | L | Y | Y | F | C | | F | L | ΔI |

Figure 19A

| Kabat | # | FR or CDR | Mouse 1D9 V _K | Mouse κ-II | Human κ-II | Human Acceptor HF-21/28 (005056) | Surface or Core | | 1D9 RK _A | 1D9 RK _B | Comment |
|-------|----|-----------|--------------------------|------------|------------|----------------------------------|-----------------|--|---------------------|---------------------|---------|
| 37 | 42 | | L | L | L | Q | c | | Q | L | Δ2 |
| 38 | 43 | | Q | Q* | Q | | c | | Q | Q | |
| 39 | 44 | | R | K | K | | c | | R | R | |
| 40 | 45 | | P | P* | P | | s | | P | P | |
| 41 | 46 | | G | G* | G | | s | | G | G | |
| 42 | 47 | | Q | Q | Q | | c | | Q | Q | |
| 43 | 48 | | S | S* | S | | c | | S | S | |
| 44 | 49 | | P | P* | P | | C | | P | P | |
| 45 | 50 | | K | K | Q | R | c | | R | R | |
| 46 | 51 | | R | L | L | | C | | R | R | |
| 47 | 52 | | L | L* | L | | C | | L | L | |
| 48 | 53 | | I | I* | I | | C | | I | I | |
| 49 | 54 | FR2 | Y | Y | Y | | C | | Y | Y | |
| 50 | 55 | CDR2 | L | K | L | | c | | L | L | |
| 51 | 56 | | V | V | V | K | c | | V | V | |
| 52 | 57 | | S | S | S | | c | | S | S | |
| 53 | 58 | | K | N | N | | c | | K | K | |
| 54 | 59 | | L | R | R | N | c | | L | L | |
| 55 | 60 | | D | F | A | R | c | | D | D | |
| 56 | 61 | CDR2 | S | S* | S | | s | | S | S | |
| 57 | 62 | FR3 | G | G | G | | S | | G | G | |
| 58 | 63 | | V | V | V | | C | | V | V | |
| 59 | 64 | | P | P | P | | C | | P | P | |
| 60 | 65 | | D | D* | D | | S | | D | D | |
| 61 | 66 | | R | R | R | | C | | R | R | |
| 62 | 67 | | F | F* | F | | C | | F | F | |
| 63 | 68 | | T | S | S | S | C | | S | S | |
| 64 | 69 | | G | G* | G | | C | | G | G | |
| 65 | 70 | | S | S* | S | | C | | S | S | |
| 66 | 71 | | G | G* | G | | C | | G | G | |
| 67 | 72 | | S | S* | S | | s | | S | S | |
| 68 | 73 | | G | G* | G | | C | | G | G | |
| 69 | 74 | | T | T* | T | | C | | T | T | |
| 70 | 75 | | D | D* | D | | C | | D | D | |
| 71 | 76 | | F | F* | F | | C | | F | F | |
| 72 | 77 | | T | T* | T | | c | | T | T | |
| 73 | 78 | | L | L | L | | c | | L | L | |
| 74 | 79 | | K | K | K | | c | | K | K | |
| 75 | 80 | | I | I | I | | c | | I | I | |
| 76 | 81 | | S | S | S | | c | | S | S | |
| 77 | 82 | | R | R* | R | | s | | R | R | |
| 78 | 83 | | V | V | V | | c | | V | V | |
| 79 | 84 | | E | E | E | | s | | E | E | |
| 80 | 85 | | A | A* | A | | c | | A | A | |
| 81 | 86 | | E | E* | E | | s | | E | E | |
| 82 | 87 | | D | D* | D | | c | | D | D | |
| 83 | 88 | | L | L | V | V | c | | V | V | |
| 84 | 89 | | G | G* | G | | c | | G | G | |
| 85 | 90 | | V | V | V | | c | | V | V | |
| 86 | 91 | | Y | Y* | Y | | c | | Y | Y | |
| 87 | 92 | | Y | Y | Y | | C | | Y | Y | |
| 88 | 93 | FR3 | C | C | C | | C | | C | C | |

Figure 19B

| Kabat | # | FR or CDR | Mouse 1D9 V _K | Mouse κ-II | Human κ-II | Human Acceptor HF-21/28 (005056) | Surface or Core | | 1D9 RK _A | 1D9 RK _B | Comment |
|-------|-----|-------------|--------------------------|------------|------------|----------------------------------|-----------------|---|---------------------|---------------------|---------|
| 89 | 94 | CDR3 | W | F | M | c | | W | W | | |
| 90 | 95 | | Q | Q* | Q | c | | Q | Q | | |
| 91 | 96 | | G | G | A | c | | G | G | | |
| 92 | 97 | | T | T | L | c | | T | T | | |
| 93 | 98 | | H | H | Q | c | | H | H | | |
| 94 | 99 | | F | V | x | s | | F | F | | |
| 95 | 100 | | P | P* | P | W | c | P | P | | |
| 95A | | | - | P | R | | | - | - | | |
| 95B | | | - | - | - | | | - | - | | |
| 95C | | | - | - | - | | | - | - | | |
| 95D | | | - | - | - | | | - | - | | |
| 95E | | | - | - | - | | | - | - | | |
| 95F | | | - | - | - | | | - | - | | |
| 96 | 101 | | Y | Y | x | c | | Y | Y | | |
| 97 | 102 | CDR3 | T | T* | T | F | c | T | T | | |
| 98 | 103 | FR4 | F | F* | F | C | | F | F | | |
| 99 | 104 | | G | G | G | c | | G | G | | |
| 100 | 105 | | G | G | Q | Q | c | Q | <u>G</u> | | |
| 101 | 100 | | G | G | G | c | | G | G | | |
| 102 | 106 | | T | T | T | c | | T | T | | |
| 103 | 107 | | K | K* | K | R | s | R | R | | |
| 104 | 108 | | L | L | V | c | | L | L | | |
| 105 | 109 | | E | E | E | s | | E | E | | |
| 106 | 110 | | I | I | I | s | | I | I | | |
| 106A | | | - | - | - | | | - | - | | |
| 107 | 111 | FR4 | K | K* | K | - | s | K | K | | |
| | | | | | | | | | | | |
| | | | | | | | | | | | |

Figure 19C

| Kabat | # | FR or CDR | Mouse 1D9 V _H | Mouse IIIc | Human III | Human Acceptor 4B4'CL (000490) | Surface Or Core | | 1D9 RH _A | 1D9 RH _B | Comment |
|-------|----|-----------|--------------------------|------------|-----------|--------------------------------|-----------------|--|---------------------|---------------------|---------|
| 1 | 1 | FR1 | E | E* | E | | s | | E | E | |
| 2 | 2 | | V | V | V | | c | | V | V | |
| 3 | 3 | | Q | K* | Q | | s | | Q | Q | |
| 4 | 4 | | L | L* | L* | | c | | L | L | |
| 5 | 5 | | V | E | V | | s | | V | V | |
| 6 | 6 | | E | E | E | | c | | E | E | |
| 7 | 7 | | S | S | S* | | c | | S | S | |
| 8 | 8 | | G | G | G* | | c | | G | G | |
| 9 | 9 | | G | G | G* | | c | | G | G | |
| 10 | 10 | | G | G* | G | | c | | G | G | |
| 11 | 11 | | L | L | L | | s | | L | L | |
| 12 | 12 | | V | V* | V | | c | | V | V | |
| 13 | 13 | | Q | Q | Q | K | s | | K | K | |
| 14 | 14 | | P | P | P* | | c | | P | P | |
| 15 | 15 | | K | G | G* | G | s | | G | G | |
| 16 | 16 | | G | G | G | | s | | G | G | |
| 17 | 17 | | S | S | S* | | c | | S | S | |
| 18 | 18 | | L | M* | L* | | c | | L | L | |
| 19 | 19 | | K | K* | R | R | c | | R | R | |
| 20 | 20 | | L | L | L | | c | | L | L | |
| 21 | 21 | | S | S | S* | | c | | S | S | |
| 22 | 22 | | C | C | C* | | c | | C | C | |
| 23 | 23 | | A | V | A | | c | | A | A | |
| 24 | 24 | | A | A | A | | c | | A | A | |
| 25 | 25 | | S | S | S* | | c | | S | S | |
| 26 | 26 | | G | G | G | | c | | G | G | |
| 27 | 27 | | F | F | F* | | c | | F | F | |
| 28 | 28 | | S | T* | T | T | c | | T | S | Δ1 |
| 29 | 29 | | F | F* | F | | c | | F | F | |
| 30 | 30 | FR1 | N | S | S | S | s | | S | N | Δ2 |
| 31 | 31 | CDR1 | A | N | S | N | c | | A | A | |
| 32 | 32 | | Y | Y | Y | A | s | | Y | Y | |
| 33 | 33 | | A | T | A | W | s | | A | A | |
| 34 | 34 | | M | M | M | | c | | M | M | |
| 35 | 35 | | N | N | S | S | c | | N | N | |
| 35a | | | - | - | - | | c | | - | - | |
| 35b | | CDR1 | - | - | - | | c | | - | - | |

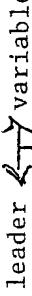
Figure 20A

| Kabat | # | FR or CDR | Mouse 1D9 V _H | Mouse IIIc | Human III | Human Acceptor 4B4'CL (000490) | Surf-ace Or Core | | 1D9 RH _A | 1D9 RH _B | Comment |
|-------|----|-----------|--------------------------|------------|-----------|--------------------------------|------------------|--|---------------------|---------------------|---------|
| 36 | 36 | FR2 | W | W | W* | | C | | W | W | |
| 37 | 37 | | V | V | V* | | C | | V | V | |
| 38 | 38 | | R | R | R* | | C | | R | R | |
| 39 | 39 | | Q | Q | Q* | | c | | Q | Q | |
| 40 | 40 | | A | S | A | | c | | A | A | |
| 41 | 41 | | P | P | P | | s | | P | P | |
| 42 | 42 | | G | E | G* | | s | | G | G | |
| 43 | 43 | | K | K | K | | s | | K | K | |
| 44 | 44 | | G | G | G | | c | | G | G | |
| 45 | 45 | | L | L | L* | | C | | L | L | |
| 46 | 46 | | E | E* | E | | C | | E | E | |
| 47 | 47 | | W | W | W* | | C | | W | W | |
| 48 | 48 | | V | V* | V* | | C | | V | V | |
| 49 | 49 | FR2 | A | A | S | G | C | | <u>G</u> | <u>G</u> | |
| 50 | 50 | CDR2 | R | E | V | | c | | R | R | |
| 51 | 51 | | I | I | I | | c | | I | I | |
| 52 | 52 | | R | R | S | K | s | | R | R | |
| 52a | 53 | | T | L | G | S | s | | T | T | |
| 52b | 54 | | K | K | K* | | s | | K | K | |
| 52c | 55 | | N | S | T | T | c | | N | N | |
| 53 | 56 | | N | H | D | D | | | N | N | |
| 54 | 57 | | N | N | G | G | | | N | N | |
| 55 | 58 | | Y | Y | G | G | | | Y | Y | |
| 56 | 59 | | A | A | S | T | s | | A | A | |
| 57 | 60 | | T | T | T | | c | | T | T | |
| 58 | 61 | | Y | H | Y | D | c | | Y | Y | |
| 59 | 62 | | Y | Y | Y | | c | | Y | Y | |
| 60 | 63 | | A | A | A | | c | | A | A | |
| 61 | 64 | | D | E | D | A | s | | D | D | |
| 62 | 65 | | S | S | S | P | s | | S | S | |
| 63 | 66 | | V | V | V* | | c | | V | V | |
| 64 | 67 | | K | K | K | | s | | K | K | |
| 65 | 68 | CDR2 | D | G | G* | G | s | | D | D | |
| 66 | 69 | FR3 | R | R | R* | | C | | R | R | |
| 67 | 70 | | Y | F | F* | F | C | | <u>F</u> | <u>F</u> | |
| 68 | 71 | | T | T | T | | C | | T | T | |
| 69 | 72 | | I | I* | I* | | C | | I | I | |
| 70 | 73 | | S | S | S* | | S | | S | S | |
| 71 | 74 | | R | R | R* | | C | | R | R | |
| 72 | 75 | | D | D | D | | c | | D | D | |
| 73 | 76 | | D | D | N | | C | | D | D | |
| 74 | 77 | | S | S | S | | s | | S | S | |
| 75 | 78 | | E | K | K | K | s | | <u>K</u> | <u>K</u> | |
| 76 | 79 | | S | S | N | N | s | | N | N | |
| 77 | 80 | | M | S | T | T | c | | <u>T</u> | <u>T</u> | |
| 78 | 81 | | L | V | L | | C | | L | L | |
| 79 | 82 | | F | Y | Y | Y | c | | <u>Y</u> | <u>Y</u> | |
| 80 | 83 | | L | L | L* | | c | | L | L | |

Figure 20B

| Kabat | # | FR or CDR | Mouse 1D9 V _H | Mouse IIIc | Human III | Human Acceptor 4B4'CL (000490) | Surface Or Core | 1D9 RH _A | 1D9 RH _B | Comment |
|-------|-----|-----------|--------------------------|------------|-----------|--------------------------------|-----------------|---------------------|---------------------|---------|
| 81 | 84 | | Q | Q* | Q | | c | Q | Q | |
| 82 | 85 | | M | M | M* | | C | M | M | |
| 82a | 86 | | N | N | N | | s | N | N | |
| 82b | 87 | | N | N | S | S | s | S | S | |
| 82c | 88 | | L | L | L* | | c | L | L | |
| 83 | 89 | | K | R | R | | s | K | K | |
| 84 | 90 | | T | A | A | | c | T | T | |
| 85 | 91 | | E | E | E | | s | E | E | |
| 86 | 92 | | D | D | D | | C | D | D | |
| 87 | 93 | | T | T | T | | c | T | T | |
| 88 | 94 | | A | G | A* | | c | A | A | |
| 89 | 95 | | M | I | V | V | c | V | V | |
| 90 | 96 | | Y | Y | Y* | | c | Y | Y | |
| 91 | 97 | | Y | Y | Y* | | C | Y | Y | |
| 92 | 98 | | C | C* | C* | | C | C | C | |
| 93 | 99 | | V | T | A | T | C | T | T | |
| 94 | 100 | FR3 | T | T | R | | C | T | T | |
| 95 | 101 | CDR3 | F | G | G | D | c | F | F | |
| 96 | 102 | | Y | F | R | S | c | Y | Y | |
| 97 | 103 | | G | - | x | L | s | G | G | |
| 98 | 104 | | N | - | G | P | c | N | N | |
| 99 | | | - | - | x | P | c | - | - | |
| 100 | | | - | - | S | H | c | - | - | |
| 100 a | | | - | - | L | | C | - | - | |
| 100 b | | | - | - | S | | C | - | - | |
| 100 c | | | - | - | G | | | - | - | |
| 100 d | | | - | - | x | | | - | - | |
| 100 e | | | - | - | Y | | | - | - | |
| 100 f | | | - | - | Y | | | - | - | |
| 100 g | | | - | - | Y | | | - | - | |
| 100 h | | | - | - | Y | | | - | - | |
| 100 i | | | - | - | H | | | - | - | |
| 100 j | | | - | - | Y | | | - | - | |
| 100 k | | | - | F | F | | C | - | - | |
| 101 | 105 | | G | A | D | R | C | G | G | |
| 102 | 106 | CDR3 | V | Y | Y | | C | V | V | |
| 103 | 107 | FR4 | W | W | W* | | C | W | W | |
| 104 | 108 | | G | G | G* | | C | G | G | |
| 105 | 109 | | T | Q | Q | Q | S | Q | Q | |
| 106 | 110 | | G | G | G* | | C | G | G | |
| 107 | 111 | | T | T | T* | | C | T | T | |
| 108 | 112 | | T | L | L | L | C | L | L | |
| 109 | 113 | | V | V | V* | | C | V | V | |
| 110 | 114 | | T | T | T* | | C | T | T | |
| 111 | 115 | | V | V* | V* | | | V | V | |
| 112 | 116 | | S | S | S* | | | S | S | |
| 113 | 117 | FR4 | S | S | S* | | | S | S | |

Figure 20C

ATGGACTTCGGTTAAACTTGGTTCTTGTGTTTATAAAGGTGTGCATTGTGAGGTGCAGCTTGTGAGTCGGAGGATTGGTGCAGCCTA
TACCTGAAGCCCAATTGAAACCAAAAGAACAAACAAAAAAATAGTTCCACACGTAACACTCCACACGTCGAACAAACTCACACCTCCCTAAACCACGTGGAT
leader  variable 100

M D F G L N L V F F V V F Y Q G V H C E V O L V E S G G L V Q P

AAGGGTCAATTGAAACCTCTCATGGCAGCCCTGGATTCACTGCGCTTCAATGCCATGAACCTGGGTCGGCAGGCTCCAGGAAAGGGTTGGATGGT
TCCCAGTAACCTTGAGAGTACACGTGGAGACCTAAGTCGAAGTTACGGGATGGGTACTTGACCCAGGGGGTCGAGGTCCATTGAGGTCTCTACTAAGTCAGGTTTACAGAG
K G S L K L S C A A S G F S F N A Y A M N W V R O A P G K G L E W V
TGCTCGCATAAAGAACTAAATAATAATTATGCCAACATAATTATGCCGATTCACTGAAAGACAGATAACCCATCTCCAGAGATGATTCAAGAAAGTATGCCTC
ACGAGCGTATTCTTGATTTTATTATAACGTTGATAATAACGGCTAAGTCACTTCTGTCTATGTGGTAGAGGTCTCTACTAAGTCAGGTTTACAGAG
A R I R T K N N N Y A T Y Y A D S V K D R Y T I S R D D S E S M L
TTCTTGCAAATGAAACCAACTTGGAAACTGAGGACACAGCCATGATTACTGTGACCTTTACGGTAACGGTGTGGGGCACAGGGACCAAGGTCAACCG
AAAGACGTTTACTTGTGAACCTTGTGACTCTTGACTCCCTGTGCGGTACATAATGACAACACTGGAAAATGCCATTGAAAAATGCCATTGCAAGTGGC
variable  constant 400

F L O M N N L K T E D T A M Y Y C V T F Y G N G V W G T G T T V T
TCTCCCTAGCCAAACAAACAGCCCCATCCGTCTATCCCTGGT
AGAGGAGTCGGTTTGTGTCGGGTAGGCAGATAGGGACCA
variable  constant 443

V S S A | K T T A P S V Y P L V

Figure 21

Docket No.: 1855.1052-028
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, et al.

A T G A A G T T G C C T I G T T A G G C T G T T G G A T T C G G G A C A A T C G G G C A T G T G A T G A C C C A G A C T C C A C T C A C T T G T G G T T A C C G T G G A C 100
T A C T T C A A C G G A C A A T C C G A C A A C C A G A C C T A A G C C C T C I G T T A G C C G C T A C A A C A C T A C T G G G T C T G A G G T G A G G T G A G G T G A A A C G C C A A T T G C C A A C C T G
M K L P V R L L V L W I R E T I G D V V M T O T P L T L S V T V G
A C C C A G G C T C C A T C T C T T G C A A G T C A A G T C A A G T C A A G G C C T C T T A G A T A G I G A T G G A A M A G A C A T T T G A A U T G G T T G I T I A C A G A G G C C A G G C C A G T C T C C C A A A 200
T G G G T C G G A G G T A G A G A A C G T T C A G T T C A G T T C A G T T C A G T T C A G T T C A G T T C A G T T C A G T T C A G T T C A G T T C A G T T C A G A G G T T T
H P A S I S C K S S Q S L L D S D G K T F L N W L L Q R P G Q S P K
G G G C C T A A T C T A T C T G G T G I C T A A A C T C G G A C T C T G G A G G T C C C T G A C A G G T T C A C T T G G C A G T G G A T C A G G G A C A G A T T C A C A T G A A A A T C A G C A G A G T G 300
C G G G A T T A G A C C A C A G A T T G A C C T G A G A C C T C A G G G A C T C A C T G C C C T G C A C T G A C T T G A C T T T G A C T T T G A C T T T G A C T T T G A C T T T G A C T T T G A C 400
R L I Y L V S K L D S G V P D R F T G S G T D F T L K I S R V
G A G G C T G A G G A T T T G G A G G T T T A T T G C T G G C A A G G T A C A C T T T C C G T A C A C G T T C G G A G G G G G A C C A A G G T G G A A A T A A A A C G G G C T G A T G C T G
C T C C G A C T C T A A A C C T C A A A T A A A C G A C C G T T C C A T G T G T A A A G G C A T G T G C A A G G C T T C C C C T G G T T C G A C C T T T A T T T G C C C G A C T A C G A C 500
variable ← → constant
E A E D L G V Y Y C W O G T H F P Y T F G G G T K L E I K R | A D A
C A C C A A C T G T A T C C A T C T T C C C A C C A 426
G T G G T T G A C A T A G G T G A A G G G T G G T
A P T V S I F P P

Figure 22

GAGGTGCAAATTGGTIGAGTCGGAGGATTGGTAAGCCCTGGGGCATTTGAGACTCTATGTGAGCCTCTGGATTCACTTCACTTGAACTGCCTACGCCA
CTCCACGTTAACCAACTAGAACCTCCTTAACCACCTGGACCCCCAGTAACCTGAGAGTACCGTGGAGACCTAAAGTGAAGTACGGATGGGT 10

E V O L V E S G G L V K P G G S L R L S C A A S G F T F S A Y A

TGAACCTGGTCCGCAGGCCTCAGGAAGGGTTGGAAATGGGTGGCCATAAGAACTAAAAAAATTAAATTGCAACATATTATGCCGATTAGTGAA
ACTTGACCCAGGGGTCCGAGGTCCTCCAAACCTTACCCAACCGGGTATTCTTGATTTTTACGTTGATAATACGTTGATAATGACATGGTGG 20

M N W V R Q A P G K G L E W V G R I R T K N N N Y A T Y Y A D S V K

AGACAGATTCACCACTCCAGAGATGATTCAAAAACACGCCCTATCTGCAAATGAACAGCTTGAAACTGAGGACACAGCCGTGTTACTGTACCC
TCTGTCTAAGTGGTAGAGGTCTTACTAAGTTTGTGCAACTTGTGAACTTTGACTTGTGCGCACATAATGACATGGTGG 30

D R F T I S R D D S K N T L Y L Q M N S L K T E D T A V Y Y C T T

B1P1

TTTACGGTAACGGTCTGGGCCAGGGACCCGGTACCGTCAGCTCAGCCAA
AAAATGCCATTGCCACAGACCCCCGGTCCCCTGGGACCAAGGGCAGTCAGTCGGTT 357

F Y G N G V W G O G T L V T V S S A K

Figure 23

Docket No.: 1855.1052-028
Title: Humanized Anti-CCR2 Antibodies...
Inventors: Gregory J. LaRosa, et al.

Figure 24